REMARKS

Claims 37 and 39-56 were previously pending. Claim 37 has been amended. No claims have been added or canceled. Claims 37 and 39-56 are pending with claim 37 being independent. No new matter is introduced.

Rejections Under 35 U.S.C. §112, First Paragraph

The Examiner rejected claims 37 and 39-56 under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement.

The Examiner has maintained the rejection of the claims of record under 35 U.S.C. §112. Pages 2-10 of the Office Action dated April 24, 2006 repeat the rejection found in the Office Action dated October 7, 2005. Pages 10-16 of the Office Action address the Examiner's reasons for maintaining the rejection for lack of enablement. Each of these issues is addressed herein. The reasons for maintaining the rejection are addressed first.

Response to the Examiner's reasons for maintaining the rejection:

a. According to the Office Action, the claims are too broad.

The only rebuttal to the arguments presented by Applicants is that the examples cited by Applicants "do not enable the scope of the very broad genus of any and all immunostimulatory oligonucleotides and any and all vaccines as presently claimed invention." (Office Action page 10).

Applicants cannot possibly rebut this rejection. A simple conclusion that all of the data presented by Applicants is not sufficient to enable the scope of the invention because the invention is broad is not adequate grounds for maintaining the rejection of record. Applicants re-iterate below all of the arguments presented in order to overcome the rejection of record.

It is further stated in the Office Action that:

> "Applicants have asserted that the key conclusions of Threadgill et al have been refuted by other investigators. Applicants have also asserted that post filing references may be used by Applicant to rebut the Examiner's assertions that the invention was unpredictable by demonstrating that the claimed invention is functional as described by Applicant in the patent application. However, claimed

> invention must be enabled as of the filing date of the patent application, not enabled by publications post filing." (Office Action page 11)

Applicants have not asserted that the invention is enabled by post-filing references. Applicants have asserted that the invention is enabled as of the date the application was filed and has pointed to data and description in the specification to support this assertion. Post filing references are used only to rebut the Examiner's claims of unpredictability of the invention which are based on post-filing references. It is respectfully requested that the reasons for maintaining the rejection of record be provided.

On page 14 of the Office Action it is stated that the scope of the claims is broad. It is further stated that "it is not clear from the claims is an antigen is actually administered with the immunostimulatory oligonucleotides." Although Applicants believe that the claims were clear as written, Applicants have amended claim 37 to clarify that a vaccine is administered with the oligonucleotide. The amendment should be sufficient to clarify the issue raised by the Examiner. It is respectfully requested that the rejection be withdrawn.

b. Response to Applicants' discussion of References cited for lack of enablement.

The Examiner has cited McCluskie et al 1999 (Molecular Med. 1999, 5/5:287-300) for the proposition that biological responses to the administration of CpG containing oligonucleotides vary depending on the mode of administration and the organism. In the outstanding Office Action the Examiner has dismissed Applicants arguments presented to rebut the rejection in view of McCluskie et al because according to the Examiner

> "the pending claims do not specifically exclude plasmids, vectors or DNA vaccines. The immunostimulatory nucleic acid could be part of a DNA vaccine; the claims just recite an immunostimulatory oligonucleotide comprising..."

This is an incorrect conclusion. The claims do not encompass plasmids, vectors or DNA vaccines. The pending independent claim is directed to the use of oligonucleotides that are stabilized, having a phosphate modified backbone. As far as Applicants are aware, plasmids, vectors or DNA vaccines do not encompass a phosphate modified backbone. If the examiner is aware of some teaching to suggest that these materials encompass a phosphate modified backbone she is respectfully requested to provide such evidence to support the rejection. The issues of

predictability and therapeutic affectivity are very different for CpG oligonucleotides and DNA vaccines.

The Examiner addressed Applicants arguments in response to each of the references, Threadgill et al 1998, Krieg et al., 2000; Wohlleben et al., 2001; Kline et al., 1998; Kline et al., 2002; Weiner et al., 2000; Agrawal et al., 2000; Dziadzio et al., 2004; Satoh et al 2002; Barnes et al., 2000; Van Uden et al, 1999; and Kussebi et al 2003 in a single paragraph. The Examiner summarized Applicants arguments as stating that each of these references shows the promise of CpG therapy and then concludes that "still...the scope of the claimed method is not enabled" (Office Action, Page 15). This is a mischaracterization of Applicants arguments. In the previous communication, Applicants rebutted the argument for each of the cited references, demonstrating that the teachings cited for lack of enablement were irrelevant, taken out of context or missing altogether. In the instances where it was applicable, Applicants also pointed out where the references were consistent with the teachings of the instant invention. This, however, did not form the basis of Applicants arguments. The Examiner is respectfully requested to respond to every aspect of the rebuttal. Each is re-iterated below for the record.

In the previous communication dated January 9, 2006, Applicants provided a number of references to demonstrate that the CpG is well tolerated in humans as well as the efficacy of the CpG in stimulating immune response in such subjects. In response, the Examiner has argued that the references are all post-filing.

Applicants cited these publications to demonstrate that CpG ODN are well tolerated and effective in stimulating an immune response in human subjects. Applicants assert that the references provided, which are indeed post-filing, serve to rebut the assertions made by the examiner that the use of CpG is associated with safety problems, and not to be intended to add new matter to the application. Therefore, the references were not provided to establish enablement; rather, they establish that the rejection with respect to lack of safety should be withdrawn. The Examiner has also indicated that copies of the references were not provided. Applicants will enclose copies of the references with an IDS.

Therefore, the Examiner has not demonstrated legal basis for lack of enablement, other than stating that there are no working examples. Since working examples are not required for determining patentability, together with the fact that general effects of CpG immunostimulatory nucleic acids are well known in the art, the examiner has not met her burden of showing lack of enablement in the instant case. Accordingly, it is respectfully requested that the rejection under § 112 be withdrawn.

Rejections repeated from prior office action but not addressed:

As discussed above, the Examiner re-iterated most of the rejections under 35 USC 112 presented in the prior Office Action dated October 7, 2005. Other than the specific points discussed above, the Examiner has not addressed any of Applicants' arguments filed in response to the Office Action dated October 7, 2005. In particular, the Examiner has addressed the issue of McCluskie et al. However, none of the points raised by Applicants in the prior response related to the remaining cited papers have been addressed. Thus, Applicants present arguments to address each of these rejections again. It is specifically requested that the Examiner address each of Applicants' arguments or withdraw the rejections.

Claims 37 and 39-56 have been rejected under 35 U.S.C. 112, first paragraph for lack of enablement. According to the Examiner, it would have required undue experimentation for one of skill in the art to practice the invention in view of the teachings of the specification, the unpredictability of the art and the lack of working examples.

Amended claim 37 recites a method for stimulating a subjects response to a vaccine by administering an immunostimulatory oligonucleotide having an unmethylated CpG dinucleotide and a phosphate backbone modification to the subject as a vaccine adjuvant in order to stimulate a response to the vaccine. The claim requires that both an oligonucleotide and a vaccine be administered. The vaccine must be administered in order for the oligonucleotide to stimulate the subjects response to that vaccine. The specification teaches that the oligonucleotide is administered in conjunction with the vaccine. "Preferably the unmethylated CpG dinucleotide is administered slightly before or at the same time as the vaccine."

The data and description in the patent application provide a teaching to those of skill in the art that CpG containing oligonucleotides can be used as immune stimulants. The specification teaches that oligonucleotides containing an unmethylated CpG dinucleotide activate lymphocytes and are thus useful for the treatment of disease and are useful as adjuvants when administered with a vaccine (Pages 7-8 and page 21 lines 18-21). The specification sets forth a description of the types of oligonucleotides useful according to the methods of the invention (Pages 9-11), methods for making the oligonucleotides (Page s 20-21), modes of administration (Page 22 lines 12-15), and pharmaceutical carriers useful in the methods (Page 22 lines 17-25).

The specification also teaches that part of the invention involved the discovery that CpG containing oligonucleotides mimic bacterial DNA in their ability to promote an immune response. The inventors believed they discovered one of natures pathways fundamental to the immune system. This discovery is described on pages 19-20 of the specification under the heading "Teleological Basis of Immunostimulatory Nucleic Acids." It is taught that the stimulatory CpG motif, identified according to the invention, is common in microbial genomic DNA, but quite rare in vertebrate DNA. Experiments described in Example 3, in which methylation of bacterial DNA with CpG methylase was found to abolish mitogenicity, demonstrated that the difference in CpG status is the cause of immune stimulation by bacterial DNA. It is further taught that "Teleologically, it appears likely that lymphocyte activation by the CpG motif represents an immune defense mechanism that can thereby distinguish bacterial from host DNA.....*Since the CpG pathway synergizes with B cell activation through the antigen receptor, B cells bearing antigen receptor specific for bacterial antigens would receive one activation signal through cell membrane Ig and a second signal from bacterial DNA, and would therefore tend to be preferentially activated. The interrelationship of this pathway with other pathways of B cell activation provide a physiologic mechanism employing a polyclonal antigen to induce antigen-specific responses."* (emphasis added)

Additionally, The Examiner has stated that the specification is not enabling because the specification does not contain any working examples. However, Applicants have provided numerous working examples in the specification. The data in the application, including that represented in Tables 1-3, establishes that the unmethylated CpG is responsible for the immune stimulation. Many oligonucleotides were tested. The data is consistent with the broad teachings of

the invention that unmethylated CpG oligonucleotides stimulate an immune response, such as by activating B cells. The cumulative data set forth throughout the patent application strongly support the use of CpG oligonucleotides as adjuvants. For instance the following working examples are included in the specification: CpG oligonucleotide induced B cell activation as measured by ^{3}H uridine (proliferation) and IgM induction (Ab production) for instance, Table 1, Examples 1 & 2; CpG oligonucleotide induced IL-6 & IL-12 induction (*in vivo*) for instance, Example 6, paragraph spanning pages 16--17; CpG oligonucleotide induced increased MHC II cell surface induction (marker of B cell activation) for instance, page 17 lines 8-19 & Example 1; combination of CpG oligonucleotide and anti-IgM resulted in a 10 fold (synergistic) increase of lymphocyte activation for instance, data described in page 15 lines 8-18; and demonstration that CpG protects B cells (WEHI-231) against growth arrest or apoptosis induced by cross-linking of the receptor for instance, page 16 lines 21-30 & Example 7. *One of skill in the art would expect, based on these data, that CpG oligonucleotides are useful as adjuvants to stimulate an antigen specific immune response to a vaccine.* These examples correlate with the claimed method. When viewed together these examples teach one of skill in the art that unmethylated CpG oligonucleotides are useful for stimulating an antigen specific immune response. These data led the inventors to conclude that CpG oligonucleotides functioned, like bacterial DNA, by inducing B cell activation to provide a physiologic mechanism employing an antigen to induce antigen-specific responses (under the section entitled "Teleological Basis" and described above).

The Examiner had previously asked in the Office Action whether the Experiment of Example 5 was actually performed. Applicants confirmed that it was performed and the data was described in the specification on page 17 lines 9-24.

The Examiner had cited several papers, all of which have a publication date later than Applicants filing date, in support of the lack of enablement rejection and in particular in support of the argument that the state of the art at the time of the invention was unpredictable.

The Examiner has cited Threadgill et al (Vaccine 1998, 16:76-82) for the proposition that CpG oligonucleotides do not function as adequate vaccine adjuvants for bacterial polysaccharide vaccines. A pointed out in response to the prior office action, although Threadgill et al report that CpG oligonucleotides are not useful adjuvants for polysaccharides, their key conclusions have since

been refuted by other investigators. Recent reports using "normal" doses for vaccinating mice and assaying for IgG show adjuvant effects, even with a variety of polysaccharide antigens, especially when they are formulated or conjugated. References addressing these issues were discussed in Applicants prior responses.

The Examiner has confirmed that some references (Gallichan et al 2001 and Harandi et al 2004) have demonstrated that CpG functions as an adjuvant in some viral compositions. The Examiner, however, states that these teachings are not indicative of the enablement at the time of the invention. This position is inconsistent. The Examiner has cited post-filing references to demonstrate that the invention was unpredictable at the time the application was filed. Post filing references may also be used by Applicant to rebut the Examiner's assertion that the invention was unpredictable by demonstrating that the claimed invention is functional as described by Applicant in the patent application.

Krieg et al is a review article describing the uses of CpG oligonucleotides. The office action specifically points to page 524 of the reference in support of the examiner's argument that biological responses to the administration of CpG containing oligonucleotides vary depending on the mode of administration and the organism. Applicants do not see this teaching in the reference. In fact the reference teaches on page 524 that "Unlike many vaccine adjuvants that have been extremely effective in mice but disappointing in humans, CpG DNA is also highly effective in higher primates." This teaching does not support the examiner's assertion that the administration of CpG oligonucleotides varies depending on the organism. Furthermore, Krieg et al describe the usefulness of CpG oligonucleotides in producing a Th1 biased immune response. Page 524 of Krieg et al includes the following teaching:

> "These and subsequent studies have shown CpG DNA to be a more effective Th1-like adjuvant than complete Freund's, and to be effective with multiple types of antigens and routes of immunization including mucosal immunization (reviewed in Ref. 50). In fact, in a comparison of 19 different adjuvants, CpG DNA was found to be the strongest for inducing Th1-like immune response to tumor antigens[51]"

The Examiner has cited Wohleben et al (TRENDS in Immunology, 2001 22/11:618-626) in support of 2 arguments: 1) that the "state of the art questions whether 'CpG-ODNs can be used in humans to inhibit the development of asthma?'" and 2) that Wohleben teaches that "all approaches that induce Th1 responses have the potential side-effects of Th1cell-mediated inflammation potentially causing serious tissue damage." The applicants respectfully disagree with the Examiner's characterization of the reference.

The pending claims do not encompass a method for treating asthma. Regardless, Wohleben et al actually provides a favorable view of CpG oligonucleotides and their usefulness in the treatment of asthma. The use of CpG oligonucleotides is identified in the abstract and conclusion of the paper as one of "the most promising approaches" for the treatment of atopic disease and particularly asthma. Even the cited paragraph on page 620 relates to the expectation that CpG oligonucleotides will be effective in humans. It is taught that the "results obtained from animal models suggest that it is probable that these approaches might also be successful in humans to reduce the development of atopic disorders." (Page 620 second column first paragraph, emphasis added) and "This suggests that the treatment of humans with CpG-ODNs could be very effective in inhibiting the development of asthma." (Page 620 second column first paragraph). Thus, the teachings found in Wohleben et al are not sufficient evidence that the invention was not enabled at the time of filing of the patent application.

Further, the teachings of Wohleben et al with respect to potential side effects do not support a lack of enablement of the claims. Wohleben et al teach on page 620 immediately following the discussion of side effects that "it is totally unclear if this can also occur in healthy rodents or, more importantly, humans." (Page 620 second column first paragraph). Additionally the issue of whether a drug is safe and has no side effects is not an appropriate test for enablement. MPEP2164.01(c). "The applicant need not demonstrate that the invention is completely safe." In fact, one cannot possibly determine the parameters of safety without a controlled clinical trial, and it is well established that a clinical trial is not required for enablement.

Furthermore, the Wohleben et al reference, as well as the others cited for safety concerns and discussed in more detail below, do not suggest that use of CpG would be unsafe. All drugs have some side effects. The references at best suggest that care should be taken to see if there may

be certain patients for which the compound might be contraindicated. This is the type of inquiry made by those of ordinary skill in the art respecting all drugs. There is no evidence in any of the cited papers that CpG oligonucleotides would be unsuitable for use as an adjuvant. To the contrary, the cited papers, published years after the filing date, continue to support the view that CpG oligonucleotides should be advanced through clinical trials for use as adjuvants. One of ordinary skill in the art would have believed, based on the data in the application, that CpG oligonucleotides would be well suited as clinical trial candidates for use as adjuvants. The papers cited for safety issues have not altered that view.

The Examiner has cited the Kline et al 2002 (Am. J. Physiol. Lung Cell Mol. Physiol., 2002, 283:L170-L179) and Kline et al 1998 (J Immunol 1998, 160: 2555-2559) references to demonstrate that the use of CpG alone in some instances is not effective for the treatment of asthma. Applicants reiterate that the pending claims are not directed to the use of CpG oligonucleotides to treat asthma nor to the use of CpG oligonucleotides alone. The claimed invention is directed to the use of CpG with a vaccine. However, since the references were made of record, Applicants address the rejection. The Examiner asserts that Kline 2002 teaches that a single treatment of CpG-ODN alone was ineffective in reducing the manifestations consistent with asthma in this animal model. The section of the paper identified by the Examiner on page L172 relates to an experiment designed to model "persistent asthma in humans, who, by current standards of treatment, require intensive anti-inflammatory therapy." The claimed invention does not require that any form of asthma, including persistent asthma be treated with a single dose of CpG. Doses are within the purview of those skilled in the art, and the data in the paper supports that monotherapy at appropriate doses can work. In fact, many drugs including other drugs for treating chronic asthma are not effective as a single dose.

The Examiner has also indicated that Kline 2002 teaches that "splenocytes from OVA-treated mice did not develop an antigen specific Th1 phenotype. However mice treated with CpG ODN and OVA had a marked shift toward a Th1 response to antigen as well as reduction in airway eosinophilia, serum IgE and bronchial hyperreactivity (p. L176, col. 2)." This statement does not support a lack of enablement of the claimed invention. The lack of development of a Th1 phenotype in mice in response to OVA treatment is not inconsistent with the invention. The fact

that CpG oligonucleotides produced a shift towards a Th1 response is consistent with Applicants' findings.

Weiner (J. Leukocyte Biology, 2000, 68:456-463) is cited for the proposition that the molecular mechanism of CpG is unknown. Knowledge of the mechanism of action isn't necessary, particularly in view of the detailed knowledge at the time the patent application was filed of the cellular effects of CpG oligonucleotides. The patent application identifies consistent changes in the immune system at the cellular level that occur in response to CpG administration and which are therapeutically relevant. Additionally, Table 1 of Weiner lists examples of cellular effects arising from immunostimulatory CpG ODN. A lack of understanding of the molecular mechanism does not render the cellular results unpredictable. Other statements in Weiner are consistent with enablement of the claimed invention. For instance it is taught on page 456 1st column second full paragraph that "Studies to date suggest CpG DNA could have significant therapeutic promise in the treatment of a variety of disorders, including infectious disease, allergy, and cancer." Page 457 under "In vivo effects of CpG ODN" teaches that "extensive studies have been done in rodents, and some studies have been done in non-human primates. The observed *in vivo* data fits well with the *in vitro* data outlined above."

Agrawal et al (Molecular Med. Today 2000, 6:72-81) has been cited in support of the assertion that the incorporation and positioning of chemical modifications relative to the CpG dinucleotide are highly unpredictable. In particular, the examiner has identified pages 78-80 as being particularly relevant. Agrawal et al is a review article describing antisense oligonucleotides. The authors suggest on page 78 that in order to *reduce* non-antisense related activity it is best to avoid CpG motifs. The authors also indicate that if it is not possible to avoid CpG motifs, then it is possible to make one of 3 modifications to reduce the CpG activity of the oligonucleotide. One of the suggested modifications is to replace the cytosine base of the CpG with a 5-methyl cytosine base. The instant specification teaches that a CpG containing oligonucleotide has an unmethylated C in the CpG motif. Further, the cited section of Agrawal et al teaches that the proposed 3 modifications "significantly reduced side effects". Agrawal et al does not teach that immune stimulation was abolished with any of these proposed modifications, just reduced.

Hussain et al., was cited for the teaching that long term benefits of CpG therapy in allergic rhinitis are speculative. A copy of the Hussain et al reference and the complete citation were not included in the office action. Thus, Applicants cannot address the merits of the full reference. Applicants note, however, that the claimed invention is not directed to the treatment of allergic rhinitis. Thus, a teaching that use of CpG therapy in the treatment of allergic rhinitis is speculative is not relevant to the claimed invention.

Satoh et al. (Fukushima Igaku Zasshi 2002, 52/3:237-250) was cited in order to demonstrate that CpG was associated with dangerous side effects. The Satoh et al. reference is an abstract describing a study on the effects of CpG oligonucleotides administered subcutaneously to mice that are treated with DNFB. It was concluded that CpG oligonucleotides were responsible for worsening of the allergic contact dermatitis (ACD) induced by DNFB. As mentioned above with respect to Wohleben et al the issue of whether a drug is safe and has no side effects is not an appropriate test for enablement. Additionally, the teachings of the Satoh et al reference are not sufficient to establish a lack of enablement for the claimed invention. The ACD is caused by DNFB treatment. The fact that CpG oligonucleotides may contribute to type IV hypersensitivity responses initiated by DNFB does not establish that CpG oligonucleotides would cause ACD in the absence of DNFB.

Dziadzio et al (Handbook of Experimental Pharmacology 161:273-285, 2004) and Metzger et al (J. Allergy. Clin. Immunol. (104)2 Pt. 1:260-266, 1999) are both cited for the teaching that CpG ODN therapy has yet to be demonstrated in human clinical trials. Both references however summarize effects of CpG ODN, in *in vitro* and *in vivo* murine systems, which parallel those required for human therapy. Neither reference doubts that CpG ODN will be effective in humans. Dziadzio et al actually teaches that CpG ODN are encouraging as potential therapies for allergic disease. After summarizing several sets of data on page 280, Dziadzio et al teach:

> "These data suggest that ISS-ODN can induce a Th1 phenotype prior to allergen exposure. It appears that even without the presence of allergen, CpG motifs can induce a Th1 phenotype in multiple cell types including B cells, antigen-presenting cells (macrophages, dendritic cells), T cells, and NK cells. The expression of Th1 cytokines along with an upregulation of costimulatory molecules on these cells underscores the importance of ISS-ODN in Th1 and innate immune responses. The persistence of a Th1 response after antigen

> challenge in sensitized mice is encouraging as potential therapy for allergic disease." (page 280, 2nd-3rd full paragraphs).

The teachings of the references as a whole do not support a finding that the claimed invention was unpredictable at the time of filing of the patent application.

The Examiner has cited Van Uden et al (J. Allergy Clin. Immunol., 1999, 104:902-910) for the concept that each ISS has a minimum length limitation and that potential side effects associated with treatment must be considered. With respect to the section of the paper that refers to the length of ODN, the authors do not conclude that there is a specific rule for the length of the ODN. The authors hypothesize that different lengths and flanking sequences have an impact on the activity of the ODN. The patent application as filed confirms that certain motifs and lengths are preferred. However, it is believed that most unmethylated CpG containing oligonucleotide within the scope of the claims would have the ability to initiate *in vivo* a pattern of cytokine release which would drive the immune system toward a Th1 response when administered in an appropriate dosage.

The examiner quotes some language from page 907 column 2 and page 908 column 1 related to the issue of side effects associated with CpG oligonucleotide administration. Each of these statements, however, is taken out of context. After the quoted section the authors point out that such side effects have not been observed. For example, the Examiner has pointed to the statement on page 907 that "There is always the possibility of unwanted effects of the powerful immune stimulation that ISS delivers" and compared the effects of CpG with LPS In contrast to the implications from the language quoted in the office action, immediately following that paragraph the authors conclude

> "Although these reports demonstrate the possibility of shock in extreme cases of sensitization or concurrent LPS exposure, there has never been a reported case of ISS alone causing shock in any kind of healthy animal at any dose." (Page 908 column 1 lines 2-6) and
> "We and others have never observed gross inflammation in response to ISS in ODN or plasmid form in any experimental animals or humans." (page 908 first column first full paragraph)

The Examiner has also stated that Van Uden et al teaches that "ISS could cause excessive local inflammation as seen with other powerful Th1 adjuvants, such as CFA." In contrast to this statement the authors point out an experiment in which bacterial DNA complexed with CFA is injected into mice. It is concluded that

> "When the mixture is given to preautoimmune NZB/NZW F1 mice, they develop antibodies that cross-react with mammalian DNA, but surprisingly they are actually protected from their spontaneous autoimmune disease. There still are no examples of ISS directly causing any type of autoimmune disease in animal models." (page 908 paragraph bridging columns 1 and 2).

Kussebi et al., Curr. Med. Chem. – Anti inflammatory & Anti-Allergy Agents, 2003, 2: 297308 was cited for the teaching that direct conjugation of CpG-ODNs to allergenic proteins or peptides was more effective than their co-administration. Applicants did not receive a copy of the full reference. The teachings of the cited portion of the reference, however, do not render the claimed invention unpredictable. Simply because the authors found CpG conjugated to an allergen to be more effective than CpG administered separately from an allergen does not suggest that the claimed invention is unpredictable. The claimed invention encompasses the use of a CpG oligonucleotide with a vaccine antigen, whether or not the components are conjugated.

As described above, numerous examples were provided in the specification. These examples in combination with the description in the specification were sufficient to enable one of skill in the art to practice the invention over the full scope of the claims. Consistent with the descriptions, a number of studies published since the filing of the patent application have reiterated, as set forth in the specification, that CpG oligonucleotides are useful as adjuvants. Several of the clinical trials described above, Cooper et al, Halperin et al, Siegrist et al, Speiser et al, and van Ojik et al, have demonstrated, as described in the specification, that CpG oligonucleotides, when administered with a vaccine to a human, produce an antigen specific immune response.

Thus, one of ordinary skill in the art, based on the teachings in the patent application, would have reasonably expected the claimed invention to work over the full scope of the claims.

Rejections Under 35 U.S.C. §102(b)

The rejection of claims 37 and 46-54 under 35 U.S.C. 102(b) as being anticipated by Tokunaga et al. has been maintained.

The entire text of the rejection was supercopied from earlier Office Actions. The only new portion of the rejection is presented below:

"The rejection is maintained for the reasons of record. Applicants have not set forth any new arguments or evidence with regard to this rejection."

This statement is incorrect and insufficient to maintain the rejection. In response to the last office action Applicants indicated that although they disagree with the rejection Applicants amended claim 37 to incorporate a limitation of claim 38, which was currently not rejected. How can the rejection of record be maintained when a limitation previously considered by the Examiner to distinguish over the art was added to the claims?

It is respectfully requested that the rejection be withdrawn.

CONCLUSION

A Notice of Allowance is respectfully requested. The Examiner is requested to call the undersigned at the telephone number listed below if this communication does not place the case in condition for allowance. If there is a fee occasioned by this response, including an extension fee, that is not covered by an enclosed check, please charge any deficiency to Deposit Account No. 23/2825.

Dated: September 25, 2006

Respectfully submitted,

By _____

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